Canad. Med. Ass. J.
Sept. 2, 1967, vol. 97

Iron Absorption in Patients with Rheumatoid Arthritis and in Normal Subjects

M. R. VAS, M.D. and N. K. M. DE LEEUW, M.D., M.Sc., F.A.C.P.,
Montreal

THE role of iron absorption in the development of iron deficiency in patients with rheumatoid arthritis has been investigated by several workers, with controversial results.[1-6] Most authors have reported no evidence of an absorptive defect. In the majority of these reports, however, the methods employed were not well suited to the measuring of decreased absorption. We decided, therefore, to study iron absorption in rheumatoid arthritis using an isotope method[7] suitable for demonstrating decreased absorption, and to correlate the results of these studies with the hematological and clinical status of the patients.[8] For comparison, iron absorption was also measured in a group of normal subjects.

MATERIALS AND METHODS

Twenty-one patients (14 women and 7 men) with rheumatoid arthritis and 25 controls (12 women and 13 men) were investigated. Most of the control subjects were laboratory technicians and medical students.

The hematological status was evaluated by the following tests: hemoglobin concentration, packed cell volume, mean corpuscular hemoglobin concentration, reticulocyte count, corrected sedimentation rate (Wintrobe), and white blood cell and differential counts performed by routine hematological methods.[9] Erythrocyte morphology was evaluated from a blood film stained with Jenner-Giemsa. Serum iron, unsaturated iron-binding capacity and blood volume determinations (using ^{131}I-tagged albumin and corrected hematocrit) were performed by methods that have been described previously.[9] Bone marrow aspiration from the sternum or from the posterior iliac crest was performed in every patient, but not in the controls. Smears were stained with Jenner-Giemsa for morphology and with potassium ferrocyanide for evaluation of iron content, which was graded from 0 to 4+.[9]

Iron absorption was measured with some modification by the method of Bonnet, Hagedorn and Owen.[7] Fifty micrograms of ferrous ammonium sulfate was mixed with 5 μc. of ^{59}Fe ($^{59}FeCl_3$, Abbott Laboratories) and 300 mg. of ascorbic acid, and diluted to 100 ml. with double-distilled water. Two millilitres of this solution was transferred into a 15-ml. tube and served as standard for the blood samples; another 2 ml. was diluted to 25 ml. in a 50-ml. tube and served as standard for the stool specimens. Two hours after a standard breakfast of toast and coffee, the remaining 96 ml. was given as the test drink, and the next meal was delayed for three hours. Except for steroids, medication was withheld from 12 hours before to three hours after taking the ^{59}Fe solution. Stools were collected for 8 to 10 days. After that time, no radioactivity could be detected in the stools. The specimens were collected in waxed-paper containers and frozen until the collection was completed. They were then transferred into a single, weighed metal can, diluted with water, weighed and mixed thoroughly by a mechanical shaker for 15 minutes. A 25-ml. sample was transferred into a 50-ml. tube and weighed, and its radioactivity measured in a well-type scintillation counter,* and compared with that of the standard. From the weight of this sample and the weight of the collected stools, the total excreted radioactivity was calculated. The amount of ^{59}Fe which was not excreted was assumed to have been absorbed and was expressed as a percentage of the administered dose.

Serial 6-ml. blood samples were collected, the packed cells were separated, and their radioactivity was measured. From this, and from the red cell mass, determined indirectly from the plasma volume and corrected hematocrit at the end of the study, the percentage of ingested as well as of absorbed ^{59}Fe which was incorporated into the red cell mass was determined.

All patients were hospitalized during the investigation. The duration of their rheumatoid arthritis varied from one month to 30 years. The activity of the disease varied. All patients, however, had a positive latex fixation test and most patients had an increased corrected sedimentation rate. One male patient (Case 32) had had a gastrectomy four years previously. All patients were carefully screened for lesions of the gastrointestinal tract and for other causes of pathological blood loss. Three or more stools were examined for occult blood using the benzidine HCl method. Treatment consisted of physiotherapy, acetylsalicylic acid, and small doses of phenobarbital in all patients, small doses of adrenocortical steroids in four, and chloroquine in four.

From the Division of Hematology, Department of Medicine, Royal Victoria Hospital and McGill University Clinic, Montreal, Quebec.

Supported in part by National Health Research Grant No. 604-7-362.

Reprint requests to: Dr. M. R. Vas, Division of Hematology, Royal Victoria Hospital, Montreal 2, Quebec.

*Atomic Instrument Company, Cambridge, Mass., U.S.A.

TABLE I.—FEMALE RHEUMATOID ARTHRITIS PATIENTS

Case No.	Age	Duration of illness (years)	Hb. (g.%)	PCV (%)	MCHC (%)	Serum iron (μg.%)	UIBC (μg.%)	Saturation (%)	Bone marrow iron	Red cell mass (ml./kg.)	Hb. mass (g./kg.)	^{59}Fe absorbed (% of given dose)	^{59}Fe utilized (% of given dose)	*Medication
1	59	10	12.9	42	31	39	229	15	trace	22.1	8.8	11	6	
2	36	12	9.5	34	28	31	458	6	0	18.1	5.7	68	57	
3	50	2	12.4	40	31	50	302	14	trace	33.8	10.1	14	16	
4	45	3	11.1	36	31	62	229	21	2+	19.6	7.1	30	17	S
5	63	30	12.4	40	31	45	229	16	1+	27.7	11.0	58	48	
6	52	7	10.9	36	30	60	220	21	2+	33.1	11.7	20	6	
7	74	3/12	14.5	45	32	46	210	18	—	28.7	11.5	13	6	
8	56	6	12.3	39	32	69	183	28	2+	30.3	11.1	36	20	
9	56	10	9.9	33	30	26	238	10	2+	29.3	11.0	11	7	C
10	28	12	7.4	27	27	10	275	4	0	13.8	2.5	9	5	C
11	64	12	10.2	30	34	41	110	27	2+	28.0	10.5	18	5	S
12	24	7	12.5	40	31	56	165	25	2+	33.6	13.1	42	19	
13	56	4	13.5	41	32	47	265	15	2+	28.9	10.0	24	12	
14	48	1	12.1	38	32	51	128	28	3+	20.4	7.0	15	9	C
Mean:	51	8	11.5	37	31	48	240	18		26.2	9.4	26	17	

*All patients received salicylates and phenobarbital.
S = Adrenocortical steroids.
C = Chloroquine.
Hb. = hemoglobin.
PCV = Packed cell volume.
MCHC = Mean corpuscular hemoglobin concentration.
UIBC = Unsaturated iron-binding capacity.
— = Not done.

RESULTS

Hematological Status

The hematological data on the 14 women with rheumatoid arthritis and on the 12 normal women are summarized in Tables I and II. Of the 14 female patients, six had a decreased hemoglobin concentration (less than 12.0 g./100 ml.) and a decreased packed cell volume (less than 37%). The corrected sedimentation rate was elevated (more than 20 mm. in one hour) in 11 cases. All female patients had decreased serum iron (less than 80 μg. %), and 10 had decreased saturation of the iron-binding protein (less than 25%). The bone marrow showed variable erythropoietic activity with normoblastic erythropoiesis in all of the patients. Two had no stainable iron in the marrow; in the others, the iron content varied from a trace to 3+. The data for the seven men with rheumatoid arthritis and the 13 normal men are summarized in Tables III and IV. Of the seven male patients, five had a decreased hemoglobin concentration (less than 14.0 g. per 100 ml.), one had decreased packed cell volume (less than 40%), and five showed an elevated corrected sedimentation rate (more than 9 mm. in one hour). All had decreased serum iron (less than 90 μg. %) and decreased saturation of the iron-binding protein (less than 25%). Bone marrow was normoblastic in all male patients. In one marrow, no stainable iron was demonstrated, while in the others, the iron content varied from 1 to 3+.

TABLE II.—FEMALE CONTROLS

Case No.	Age	Hb. (g.%)	PCV (%)	MCHC (%)	Serum iron (μg.%)	UIBC (μg.%)	Saturation (%)	Red cell mass (ml./kg.)	Hb. mass (g./kg.)	^{59}Fe absorbed (% of given dose)	^{59}Fe utilized (% of given dose)
15	47	12.1	39	31	76	174	30	17.3	6.0*	50	18
16	28	12.1	41	30	67	183	27	25.0	8.6	52	32
17	30	14.3	45	32	98	183	35	32.1	11.2	95	80
18	23	13.5	44	31	107	275	28	26.6	10.7	63	46
19	27	14.1	45	31	100	165	38	28.0	10.5	79	41
20	37	13.3	42	32	135	146	48	25.1	9.8	73	46
21	24	13.7	43	32	82	156	34	22.9	8.8	78	64
22	25	14.3	46	31	91	156	37	26.5	10.9	82	70
23	20	13.7	44	31	114	156	41	25.3	9.9	57	20
24	28	15.0	45	34	104	137	43	20.7	8.5	45	20
25	56	13.5	43	32	85	183	32	21.2	8.1	48	11
26	54	13.7	44	31	85	156	35	22.2	8.3	42	26
Mean:	33	13.6	43	32	95	172	36	24.4	9.3	64	40

*Obese woman.

TABLE III.—MALE RHEUMATOID ARTHRITIS PATIENTS

Case No.	Age	Duration of illness (years)	Hb. (g.%)	PCV (%)	MCHC (%)	Serum iron (μg.%)	UIBC (μg.%)	Saturation (%)	Bone marrow iron	Red cell mass (ml./kg.)	Hb. mass (g./kg.)	^{59}Fe absorbed (% of given dose)	^{59}Fe utilized (% of given dose)	Medication
27	34	2	14.5	45	32	42	247	15	2+	39.2	15.1	10	1	
28	72	30	13.9	45	31	27	146	16	2+	32.0	11.9	3	6	
29	31	1/12	14.8	46	32	79	256	24	1+	28.1	10.9	38	26	
30	60	10	8.7	25	35	22	128	15	3+	25.1	8.0	37	9	S.C.
31	41	20	12.0	41	29	24	275	8	0	40.6	14.3	76	47	S
32	57	13	13.3	42	32	20	201	10	2+	32.6	12.6	35	15	
33	59	5	12.1	41	29	15	165	8	3+	41.3	15.8	42	2	
Mean:	51	11	12.8	41	31	33	202	14		34.1	12.7	34	15	

TABLE IV.—MALE CONTROLS

Case No.	Age	Hb. (g.%)	PCV (%)	MCHC (%)	Serum iron (μg.%)	UIBC (μg.%)	Saturation (%)	Red cell mass (ml./kg.)	Hb. mass (g./kg.)	^{59}Fe absorbed (% of given dose)	^{59}Fe utilized
34	76	14.1	44	32	103	82	56	29.7	10.1	32	8
35	28	15.3	48	32	93	174	35	29.5	12.8	28	19
36	29	15.1	46	33	116	146	44	29.1	11.2	14	4
37	25	14.5	45	32	100	210	32	29.7	10.5	37	20
38	26	15.1	48	32	136	165	45	26.7	10.2	26	9
39	37	15.5	49	31	121	137	47	28.9	11.1	6	3
40	28	16.0	49	33	146	183	44	33.7	13.2	24	11
41	25	14.5	45	32	74	128	37	29.3	11.6	70	27
42	25	16.4	48	36	128	82	61	33.4	13.9	30	11
43	23	14.7	45	33	101	37	72	30.8	10.7	12	4
44	24	15.5	48	32	84	229	27	—	—	22	—
45	28	16.1	48	33	110	220	33	25.3	9.8	72	64
46	25	16.4	50	33	91	128	42	36.4	14.5	30	—
Mean:	31	15.3	47	33	109	148	44	30.2	11.6	31	16

^{59}Fe Absorption Test

The results are shown in Tables I to IV. The women with rheumatoid arthritis absorbed 9 to 68% of the test dose, with a mean of 26%. This was significantly less ($p < 0.01$) than in the control women, who absorbed 42 to 96% of the test dose, with a mean of 64%. There was no significant difference in ^{59}Fe absorption between the male patients with rheumatoid arthritis (range 3 to 76%, mean 34%) and their controls (range 6 to 72%, mean 31%). The one male patient (Case 31) who absorbed 76% had iron deficiency. The patient (Case 32) who underwent gastrectomy four years previously, absorbed 35% of the radioactive iron.

Similarly, the mean percentage of *administered* ^{59}Fe which was utilized for hemoglobin synthesis was significantly less in female patients (17%) than in the control women (40%), whereas there was no such difference between male patients (15%) and their controls (16%).

The mean percentage of *absorbed* ^{59}Fe which was utilized for hemoglobin synthesis was not significantly different in female patients (59%) and their controls (61%), or in male patients (33%) and controls (45%), although there was a sex difference. Therefore, there was an excellent correlation ($R = 0.84\text{-}0.94$; $p = < 0.005\text{-} < 0.0005$) of ^{59}Fe absorption with utilization of the given dose in each of the four groups (Fig. 1).

In two female patients with iron deficiency anemia the test was repeated. (These results are not included in the tables.) One of these (Case 2) showed the highest absorption (68%) in the group. She was treated with oral iron for one year. Her hemoglobin level rose from 9.5 to 13.5 g. %, her serum iron from 31 to 76 μg. %, and the unsaturated iron-binding capacity decreased from 458 to 339 μg. %; however, her bone marrow was still depleted of iron. At that time, ^{59}Fe absorption was repeated and was 39%. The second patient (Case 10) had ingested 250 mg. of chloroquine a few minutes before the ^{59}Fe was administered. In spite of her iron deficiency state, she absorbed only 9% of the given dose. Three months later, the ^{59}Fe test was repeated, and chloroquine was withheld for 12 hours before and after the ^{59}Fe was given. In this repeated test she absorbed 50% of the radioactive iron.

^{59}Fe absorption showed no correlation with hemoglobin concentration, packed cell volume, mean corpuscular hemoglobin concentration, unsaturated iron-binding capacity, transferrin saturation, and age in any of the control or patient groups, nor was there a correlation between ^{59}Fe absorption and corrected sedimentation rate or duration of illness in the two groups of patients. Exclusion of the data of the three patients with iron deficiency did not affect the results. However, in the normal women a significant correlation ($R = 0.64\text{-}0.78$; $p = < 0.025\text{-}$

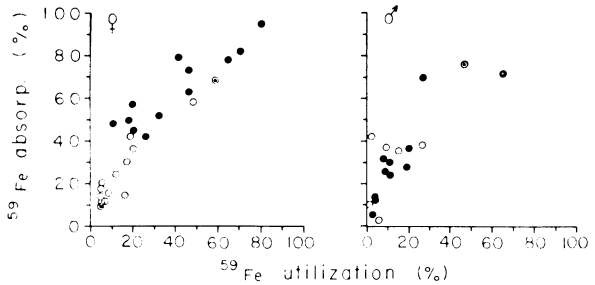

Fig. 1.—Correlation between absorption and utilization of the given dose of ^{59}Fe.
● = controls
○ = patients
⊙ = patients with iron deficiency.

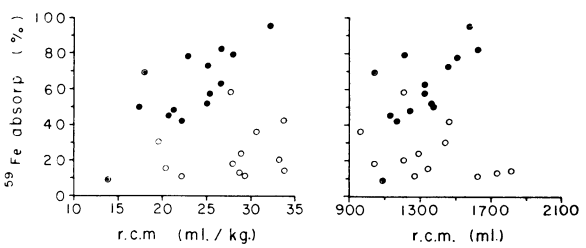

Fig. 2.—Correlation between ^{59}Fe absorption and red cell mass (in ml./kg. and in ml.) in normal women and female patients with rheumatoid arthritis.
● = controls
○ = patients
⊙ = patients with iron deficiency.
r.c.m. = red cell mass

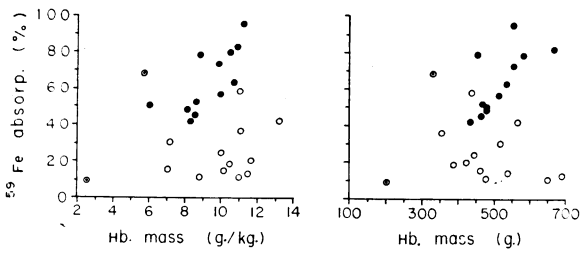

Fig. 3.—Correlation between ^{59}Fe absorption and hemoglobin mass (in g./kg. and in g.) in normal women and female patients with rheumatoid arthritis.
● = controls
○ = patients
⊙ = patients with iron deficiency.
Hb. = hemoglobin

< 0.0025) was demonstrated between ^{59}Fe absorption and red cell mass or hemoglobin mass, either per unit weight or as absolute value (Figs. 2 and 3). This correlation was not found in the group of male controls, or in the male and female patients.

Discussion

Anemia is a frequent complication of rheumatoid arthritis. The anemia is usually normocytic, normochromic or slightly hypochromic,[1, 10] rarely macrocytic.[11, 12] The serum iron is decreased and the iron-binding capacity varies.[1, 3, 4] The available data regarding the state of iron stores in this disease[6, 13-15] are contradictory. In our series, only 3 of 21 patients lacked stainable iron particles in the bone marrow and thus could be considered to have iron deficiency—an incidence of 14%. This is lower than in the series of McCrea[13] or Richmond *et al.*[15, 16] where the incidence was 33%,[13] 31%[15] and 49%,[16] respectively. Our findings are in contrast to Weinstein's report[6] in which no evidence of iron deficiency anemia was found in 20 patients. Other writers have emphasized increased bone marrow hemosiderin and a decrease in sideroblasts during the active phase of the disease.[23]

Several factors could contribute to the development of iron deficiency, such as (a) decreased iron intake, (b) blood loss and (c) impaired absorption of iron.

(a) *Decreased iron intake.*—There was no evidence of gross dietary deficiency in our patients.

(b) *Blood loss.*—In four patients occult blood was found in the stools. Each of these patients had only one positive stool of several specimens tested. Except for one (Case 1), they were iron deficient, and showed evidence of pathological blood loss; one (Case 2) had menorrhagia and the other two (Cases 10 and 31) had had bleeding hemorrhoids in the past. It has been demonstated by ^{51}Cr studies that up to 70% of patients taking salicylates lose small amounts of blood in the stool without clinical or radiological evidence of a gastrointestinal lesion.[17] Thus, it is possible that some of our patients experienced microscopic blood loss which was not detected by the usual laboratory procedures.

(c) *Impaired absorption of iron.*—This has been implicated by some authors, based on the observation that many patients with rheumatoid arthritis who do not respond to oral iron will respond to parenteral iron therapy.[5, 18] Iron absorption tests measuring the rise in serum iron after an oral dose[1, 4, 5] or their isotopic counterpart[6] were used in most previous investigations, but are not acceptable as quantitative tests of iron absorption. Isotope studies using fecal collection have given controversial results. In the one study where no impairment of absorption was found, no distinction was made between iron-deficient and iron-sufficient subjects, and the method employed was not suitable for demonstrating decreased absorption.[2] In the other study,[3] the same technique[7] was used as in the present investigation. Decreased absorption was found in four out of seven male patients and in two of five female patients. However, the data were too few to draw conclusions.*

The method chosen in the present study has the advantage that normal values are sufficiently high to allow measurement of decreased absorption. The mean values in our normal subjects compare well with those reported by Bonnet, Hagedorn and Owen.[7]

The two most important systemic determinants of iron absorption are erythropoietic bone-marrow activity on the one hand and the state of iron stores on the other.[19] Increased erythropoiesis and depletion of iron stores both cause increased iron absorption. Since there is no evidence that erythropoiesis is more active in the female than in the male, differences in iron stores must be considered to explain the greater absorption in normal women than in normal men.

It is known that the average amount of storage iron is less in women than in men.[19] Our previous data show that of 13 normal women, 11 had a trace of and two had 1+ hemosiderin in the bone marrow,[9, 20] whereas of nine normal men, four had 1+, four had 2+ and one had 3+ bone-marrow hemosiderin.[20, 21] The average

*Since this manuscript was completed, an excellent and thorough study of "Anemia in rheumatoid arthritis" by O. Strandberg was published in *Acta Med. Scand.*, Suppl. 454, 1966. In this, L. Engstedt and O. Strandberg, using a radioactive method which was slightly different from ours, have found a significantly decreased iron absorption in their female patients. Utilization of absorbed iron was the same in patients as in controls.

Canad. Med. Ass. J.
Sept. 2, 1967, vol. 97

storage iron in 10 menstruating women[22] and in a large group of pregnant women in the first trimester (before pregnancy had made any demands on the iron stores) has been calculated at approximately 300 mg.[9] Thus it is likely that in our control women iron stores were marginal and that this would account for their increased ^{59}Fe absorption. It is of interest that the *per cent* ^{59}Fe absorbed was directly related to red cell and hemoglobin mass, suggesting that iron absorption was determined *quantitatively* by the needs of the erythron. In the normal men, iron absorption apparently was not predominantly determined by the needs of the erythron since the amount of ^{59}Fe absorbed did not correlate with red cell or hemoglobin mass. If one assumes that in the group of normal men iron stores were similar to the ones in a previous investigation,[20, 21] then their iron-sufficiency state limited their iron absorption.

The female patients showed a significantly lower absorption than their healthy controls. There are several factors which could contribute to this difference:

1. *Increased iron stores.* The majority of female patients had 2+ bone marrow hemosiderin. This was more than the trace which was present in the bone marrows of the majority of normal women previously studied.[9, 20]

It is possible that the increased marrow hemosiderin in the female patients was related to the rheumatoid process,[23] even though a similar difference was not apparent between male patients and a series of previously studied healthy males.

It is also possible that the female patients had a higher iron content in their bone marrow than the control women, owing to a difference in age between the two groups[24] (Tables I and II). It would have been desirable to have a similar age distribution in female patients and controls, but from a practical standpoint it proved impossible to obtain a sufficient number of healthy control women of the same age group as the patients. However, most of the patients between 40 and 60 years of age had lower ^{59}Fe absorption than the three control women in that age group. Thus it is not likely that age difference alone can explain the decreased absorption in the female patients.

Iron administration may lead to increased iron content of the marrow; however, none of our patients were treated with iron in the past.

2. *Effect of drugs on iron absorption.* It is possible that some of the drugs which the patients were taking interfered with iron absorption either by formation of insoluble complexes as has been shown for other substances which decrease iron absorption,[19] or by affecting the intestinal mucosa. There was suggestive evidence that chloroquine decreased iron absorption in one patient. No definite correlation could be established between salicylate intake and iron absorption, although this possibility is not excluded.*

3. *Intestinal mucosal alteration.* It is conceivable that the intestinal mucosa could be altered as part of the systemic disease, causing decreased iron absorption. However, the similar findings in male patients as in their controls make this a less likely possibility.

4. *Decreased erythropoietic activity.* There was no evidence that decreased erythropoietic activity was responsible for decreased absorption in the female patients, since their mean hemoglobin mass was the same as that in the normal women (Tables I and II).

The utilization of absorbed iron for hemoglobin synthesis showed no significant difference between patients and controls, although there was better utilization in the women than in the men. Our findings are in agreement with other data in which utilization of transferrin-bound radioactive iron was found to be normal in patients with rheumatoid arthritis.[10]

Thus, it would seem that iron absorption is impaired in some but not in all patients with rheumatoid arthritis, and that the impairment is more readily demonstrable in female patients than in male patients, because of higher absorption in the control women. In the men, differences may not have been significant as a result of the lower absorption in normal males and the fewer data on male patients. Our findings are different from those of Roberts *et al.*,[3] who found decreased absorption in four of seven male patients. The causes for the impairment of ^{59}Fe absorption in the female patients may be complex. Increased storage iron may be a factor. The influence of medication on iron absorption is suggestive and warrants further investigation.

It should not be concluded that decreased iron absorption was responsible for depletion of iron stores in some patients, since in all three iron-deficient patients, pathological blood loss was demonstrated. Our findings show that when iron-deficiency anemia had developed, some patients (Cases 2 and 31) were able to absorb a large percentage of the radioactive iron. They were unable, however, to increase their absorption of food iron to compensate for their continued losses. Impaired absorption of iron from

*Recently we have observed that ^{59}Fe absorption in an iron-deficient woman with rheumatoid arthritis rose from 32% to 82% after withdrawal of salicylates for 48 hours.

nutrients may have played a role in perpetuating or aggravating the iron-deficiency state.

In recent years, a megaloblastic anemia caused by folate or vitamin B_{12} deficiency has been observed among rheumatoid patients.[11, 12] Although serum folate and vitamin B_{12} levels were not determined, no macrocytosis was noted on the blood films and bone marrow erythropoiesis was normoblastic in every patient.

Summary Iron absorption was studied in 21 patients with rheumatoid arthritis and in 25 controls. A mixture containing 5 μc. of $^{59}FeCl_3$, 50 μg. of ferrous ammonium sulfate, and 300 mg. of ascorbic acid was given orally; stools and blood samples were collected to measure ^{59}Fe absorption and utilization for hemoglobin synthesis.

Mean ^{59}Fe absorption was significantly lower in 14 female patients (26%) than in 12 normal women (63%), but it was similar in seven male patients (34%) and in 13 normal men (31%). Utilization of absorbed ^{59}Fe for hemoglobin synthesis was higher in women than in men, but there was no difference between patients and controls. A significant correlation was found between ^{59}Fe absorption and red cell mass (or hemoglobin mass) in normal women; this correlation was not found in normal men or in the patients.

It is concluded that: (1) ^{59}Fe absorption in female patients with rheumatoid arthritis is decreased; increased iron stores and the effect of drugs on iron absorption are probably important causative factors. (2) In three iron-deficient patients with evidence of gastrointestinal blood loss, the blood loss was responsible for their iron-deficiency state more than was their impaired iron absorption. (3) In normal women ^{59}Fe absorption is quantitatively determined by erythropoietic bone-marrow activity.

Résumé Nous avons étudié l'absorption du fer chez 21 arthritiques et chez 25 sujets-témoins normaux. A cet effet, nous avons administré *per os* un mélange contenant cinq microcuries du $^{59}FeCl_3$, 50 mcg de sulfate ammonique ferreux et 300 mg d'acide ascorbique; des échantillons des selles et de sang ont été recueillis en vue de mesurer l'absorption du ^{59}Fe et son utilisation pour la synthèse de l'hémoglobine.

L'absorption moyenne de ^{59}Fe a été sensiblement plus faible chez 14 malades femmes (26%) que chez 12 femmes normales (63%); elle était semblable chez sept malades hommes (34%) et chez 13 hommes sains (31%). Quant à l'utilisation du ^{59}Fe pour la synthèse de l'hémoglobine, elle était plus élevée chez les femmes que chez les hommes, mais on n'a constaté aucune différence entre les malades et les témoins. Chez les femmes normales, existait une corrélation étroite entre l'absorption du ^{59}Fe et le volume des érythrocytes (ou le volume de l'hémoglobine); cette corrélation n'a été notée ni parmi les hommes normaux, ni chez les malades.

Nous en concluons que: (1) absorption du ^{59}Fe chez les femmes souffrant d'arthrite rhumatoïde est diminuée; parmi les facteurs étiologiques, on peut probablement incriminer une augmentation des réserves de fer et l'effet de médicaments anti-arthritiques. (2) Chez trois malades avec insuffisances de fer et qui présentaient des signes d'une hémorragie digestive, la perte de sang plus que la déficience d'absorption de fer était la cause de leur état sidéroprive. (3) Chez les femmes normales, on établit quantitativement l'absorption du ^{59}Fe par l'activité érythropoïétique de la moëlle osseuse.

We are indebted to Dr. M. A. Stephens, Associate Professor of the Department of Mathematics, McGill University, for the statistical analyses; Mrs. Denise Carvalho and Mrs. Susan Hutchison for their skilful technical assistance. Dr. L. Johnson for reviewing the manuscript, and Dr. L. Lowenstein for his helpful criticism during the preparation of this manuscript.

REFERENCES

1. JEFFREY, M. R.: *Blood*, **8**: 502, 1953.
2. JEFFREY, M. R. *et al.*: *Clin. Sci.*, **14**: 395, 1955.
3. ROBERTS, F. D. *et al.*: *Blood*, **21**: 470, 1963.
4. ROY, L. M. H., ALEXANDER, W. R. M. AND DUTHIE, J. J. R.: *Ann. Rheum. Dis.*, **14**: 63, 1955.
5. SINCLAIR, R. J. G. AND DUTHIE, J. J. R.: *Brit. Med. J.*, **2**: 1257, 1950.
6. WEINSTEIN, I. M.: *Blood*, **14**: 950, 1959.
7. BONNET, J. D., HAGEDORN, A. B. AND OWEN, C. A., JR.: *Ibid.*, **15**: 36, 1960.
8. VAS, M. R. AND DE LEEUW, N. K. M.: *Canad. Med. Ass. J.*, **96**: 365, 1967 (abstract).
9. DE LEEUW, N. K. M., LOWENSTEIN, L. AND HSIEH, Y.-S.: *Medicine (Balt.)*, **45**: 291, 1966.
10. FREIREICH, E. H. *et al.*: *J. Clin. Invest.*, **36**: 1043, 1957.
11. GOUGH, K. R. *et al.*: *Brit. Med. J.*, **1**: 212, 1964.
12. PARTRIDGE, R. E. H. AND DUTHIE, J. J. R.: *Ibid.*, **1**: 89, 1963.
13. MCCREA, P. C.: *Ann. Rheum. Dis.*, **17**: 89, 1958.
14. PRATT, P. T. AND JOHNSON, M. E.: *A.M.A. Arch. Intern. Med.*, **93**: 725, 1954.
15. RICHMOND, J. *et al.*: *Ann. Rheum. Dis.*, **15**: 217, 1956.
16. RICHMOND, J. *et al.*: *Ibid.*, **17**: 406, 1958.
17. SCOTT, J. T. *et al.*: *Quart. J. Med.*, **30**: 167, 1961.
18. MILLARD, J. B. AND BARBER, H. S.: *Ann. Rheum. Dis.*, **15**: 51, 1956.
19. BOTHWELL, T. H. AND FINCH, C. A.: Iron metabolism, Little, Brown & Co. Inc., Boston, 1962.
20. DE LEEUW, N. K. M. AND LOWENSTEIN, L.: *Canad. Med. Ass. J.*, **95**: 554, 1966.
21. VAS, M. R. AND DE LEEUW, N. K. M.: Unpublished results.
22. PRITCHARD, J. A. AND MASON, R. A.: *J. A. M. A.*, **190**: 897, 1964.
23. MOURIQUAND, C. *et al.*: *Nouv. Rev. Franç. Hémat.*, **2**: 55, 1962.
24. BENZIE, R. M.: *Lancet*, **1**: 1074, 1963.